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# CHEMICAL CORPS MEDICAL LABORATORIES RESEARCH REPORT

Report No. 258

## INHALATION TOXICITY OF DIBORANE IN DOGS, RATS, AND GUINEA PIGS

by

Charles C. Comstock  
Leo Feinsilver  
Lorraine H. Lawson  
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March 1954

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**CHEMICAL CORPS  
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**Medical Laboratories Research Report No. 258**

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Inhalation Toxicity of Diborane in Dogs, Rats, and Guinea Pigs

ABSTRACT

OBJECT.

The purpose of this work was to determine the acute and chronic toxicity of diborane by inhalation to dogs, rats, and guinea pigs.

RESULTS.

1. Acute exposure.

Groups of six rats were exposed to diborane concentrations of 52 to 492 mg./m<sup>3</sup> (47 to 446 ppm) for one to four hours (Ct 10,400 to 37,200 mg. min./m<sup>3</sup>). Animals were observed for 14 days after exposure and mortality recorded. Pathological examination of animals dying as a result of gassing was performed.

2. Chronic exposure (6 hours per day, 5 days per week).

a. Two dogs and 18 rats were exposed to a diborane concentration of 6 mg./m<sup>3</sup> (5 ppm) for periods of three weeks to six months. Pathological examination of exposed animals was performed.

b. Two dogs, 20 rats and 10 guinea pigs were exposed to diborane concentrations of 0.8-1.7 mg./m<sup>3</sup> (1-2 ppm) for periods of one to six months. Pathological examination of exposed animals was performed.

CONCLUSIONS.

1. Acute exposures.

Mortality fractions of 33 to 100% were observed. As the concentration of diborane is raised there is an increasing tendency for deaths of animals to occur at short periods of time after gassing. At the two highest concentrations, 317 and 492 mg./m<sup>3</sup>, all animals died within two hours after removal from the gassing chamber.

2. Chronic exposures.

a. Exposure to 6 mg./m<sup>3</sup> of diborane resulted in death of two dogs after 10 and 25 exposures, respectively. Both dogs developed clinical signs of respiratory infection at about the ninth exposure; this diagnosis was confirmed by autopsy of the first dog.

Seventeen of 18 rats died during the course of six months exposure; deaths were distributed between the 7th and 113th exposures.

b. One dog died after 14 exposures to 0.8-1.7 mg./m<sup>3</sup> of diborane; the other survived six months of exposure. Pathological examination of the second dog revealed no changes attributable to diborane exposure.

## JCP-I, DPG

None of ten guinea pigs died during 95 exposures. Examination of animals sacrificed after 95 exposures did not reveal any changes attributable to diborane exposure.

Pathological examination of rats sacrificed after 57 exposures revealed no changes not present to a comparable degree in the control animals.

c. It is suggested that the maximum allowable concentration for chronic exposure of man to diborane be less than  $0.8 \text{ mg./m}^3$  (1 ppm).

Medical Laboratories Research Report No. 258

Inhalation Toxicity of Diborane in Dogs, Rats, and Guinea Pigs

I. INTRODUCTION.

A. Object.

The purpose of this work was to determine the acute and chronic toxicity of diborane by inhalation to dogs, rats, and guinea pigs.

B. Authority.

Authorized by the Chief Chemical Officer, under Project 4-61-14-002, Health Hazards of Military Chemicals, Cml C Research and Development Program for fiscal years, 1949, 1950 and 1951.

II. HISTORICAL.

Two reports (1,2) on toxic effects of inhaled diborane in man describe symptoms, following exposure, of fever, dizziness, headache, nausea, chest constriction, a heavy feeling in the legs and soreness of the back muscles. These symptoms disappeared after one or two hours.

Another study (3) reports 12 instances of accidental exposure to diborane incidental to its manufacture. The chief clinical symptoms were of a respiratory nature and were similar to those occurring in metal fume fever. There was delayed onset of chills and fever beginning two to three hours after removal from the environment and lasting about four hours. Some persons experienced transient tightness of the chest and a dry cough. All of these individuals appeared fully recovered within 24 hours and no permanent after effects were seen.

Other clinical studies have been made by the U. S. Public Health Service (4).

An employee of the Gassing Branch, Cml C Medical Laboratories, was exposed for 5 to 10 seconds to diborane as a result of a cylinder valve leak. A constrictive feeling in the chest was noticed immediately. This was followed in five minutes by weakness in the knees and legs. Duration of the leg weakness was only a few minutes, but the chest symptoms persisted for an hour. No other effects were noted.

Rozendaal (5) has described one case of accidental exposure to diborane in a 31-year old male. After a latent period of several hours a syndrome similar to metal fume fever developed with exhaustion, shortness of breath, chills, and fever, and a temperature rise to 104°F. Complete recovery was achieved in 3 days.

In view of the potential health hazards arising in the manufacture and use of diborane, and especially since there is no information regarding the chronic toxicity of this material, a study of the toxicological properties of diborane was initiated at a conference at Army Chemical Center on 15 July

1949 (6). As a result of this conference acute and chronic toxicity studies were carried out by exposing animals to diborane vapor. Observations were made of toxic signs, mortality of exposed animals, and pathological changes in tissues and organs.

### III. EXPERIMENTAL.

#### A. Materials and Equipment.

##### 1. Diborane Supply.

Diborane was received from the General Electric Co. in cylinders containing approximately 1/10 lb. of the compressed gas. Great care in handling this material was taken due to its inflammability and tendency to explode when mixed with air. Cylinders were stored at  $-78^{\circ}\text{C}$ . in dry ice, and other safety precautions recommended by the manufacturer were observed.

##### 2. Animals.

The animals used were albino male rats, weighing 150 to 200 grams; male beagle dogs, weighing 9 to 12 kg.; and guinea pigs, weighing 300 to 400 grams. All animals were kept in the vicinity of the gassing chambers for about two weeks prior to and throughout the tests.

##### 3. Gassing Chambers.

###### a. Acute exposures.

A glass jar of approximately  $0.02 \text{ m}^3$  capacity was used as a gassing chamber. The top was constructed of Cotoid\* painted rubber sheeting clamped to the jar by means of a metal plate. A mixture of diborane and air was drawn through the chamber at a controlled rate by use of a vacuum source and suitably constructed glass inlet and outlet tubes. The outlet tube was arranged to permit passage of the diborane and air mixture through either a decontaminating system or a series of four absorption tubes for collection of samples for diborane analysis. Two Cotoid painted circular animal racks, each large enough to accommodate three rats, were placed one above the other within the chamber. Care was taken to minimize the area of rubber tubing exposed to diborane by having each glass tubing connection placed in close contact with each other.

###### b. Chronic exposures.

A conventional dynamic flow gassing chamber of  $0.76 \text{ m}^3$  capacity was used.

\* An acid and alkali resistant paint of low adsorptive capacity manufactured by Lithgow Corporation, Chicago, Illinois.



B. Procedure.

1. Acute exposures.

Rats were exposed 1-4 hours to concentrations of 52-492 mg./m<sup>3</sup> of diborane.

The diborane and air mixture was passed through the chamber at a rate of 0.002 m<sup>3</sup>/min. When equilibrium within the chamber was established the top was removed and 6 rats, 3 on each tier, were quickly placed in the chamber for the exposure test. Animals were observed for a period of 14 days following exposure and all deaths occurring within this period were included in the determination of the mortality fraction. Pathological examination was conducted on several animals which died during or shortly after diborane exposure.

2. Chronic exposures.

Animals were exposed 6 hours per day, 5 days per week, for 3 weeks to six months. After placing the animals in the 0.76 m<sup>3</sup> chamber the diborane and air mixture was drawn through at a rate of 0.15 m<sup>3</sup>/min. At the conclusion of the 6-hour exposure the flow of diborane was terminated and the animals left in the chamber until the diborane was removed by the continuing airflow. By this procedure an attempt was made to compensate for the reduced concentration of diborane during the initial equilibration period.

a. Test 1.

Two dogs and 18 rats were exposed to a diborane concentration of 6 mg./m<sup>3</sup> for periods of three weeks to six months. One dog and 10 rats served as controls. Approximately once a week a blood sample for analysis was collected from the cephalic vein of each dog. Urine specimens were also collected every week. The following determinations were made:

(1) Whole blood: specific gravity, total red and white cell counts, differential white cell count, platelet count, hemoglobin content (7), sedimentation rate and hematocrit.

(2) Serum: chloride (8), bicarbonate (9), sugar (10), urea (11), sodium and potassium (12), cholesterol (13), calcium and phosphorus (14).

(3) Plasma: total protein (15).

(4) Urine: pH (Fisher alkacid test paper), specific gravity (hydrometer), sugar (Benedict's reagent), albumin (Robert's reagent) and microscopic examination of sediment.

b. Test 2.

Two dogs, 20 rats and 10 guinea pigs were exposed to diborane concentrations varying between 0.8-1.7 mg./m<sup>3</sup> for periods of one to 6 months. One dog and 10 rats served as controls. Blood and urine analyses were carried out as in Test 1, except that hemoglobin was determined colorimetrically by a modification of the method of Turner (16). Samples were collected monthly instead of weekly. Plasma protein concentration was not determined.

## C. Analytical Procedures.

1. Titrimetric determination of boric acid. Analytical method for diborane used in acute exposures and Test 1 of the chronic exposures.

According to Schlesinger and Burg (17) diborane reacts readily with water to form boric acid and hydrogen:  $B_2H_6 + 6H_2O \longrightarrow 6H_2 + 2H_3BO_3$ . Thus diborane chamber concentrations may be determined by measurement of the boric acid formed by hydrolysis of the diborane in a known volume of chamber air. Samples were collected at a flow rate of 0.001 m<sup>3</sup>/min. in a series of four bubblers, each containing 20 ml. of water maintained at approximately 70°C. The volume of air sampled was adjusted to yield approximately 3 mg. of boric acid after hydrolysis. After absorption of diborane the contents of the bubblers were transferred to a glass-stoppered Erlenmeyer flask containing one gram of C.P. Mannitol. The solution was boiled to expel carbon dioxide, cooled and titrated with 0.02 N sodium hydroxide, using phenolphthalein as an indicator. Blank values were determined on solutions prepared in a similar fashion without the addition of diborane.

2. Colorimetric determination of boric acid. Analytical method for diborane used in Test 2 of the chronic exposures.

Hatcher and Wilcox (18) have described a colorimetric method for the determination of boric acid based on the reaction of boric acid with the hydroxyanthraquinone dye, carmine, in concentrated sulfuric acid solution. Under these conditions a chelated colored complex is formed with an absorption maximum at 585 mμ. The absorption obeys Beer's law in the range 0 to 20 micrograms of boron in 22 ml. of solution. Chamber air samples were collected at a rate of 0.0014 m<sup>3</sup>/min. in an absorption column containing glass beads and 15 ml. of ethyl cellosolve (19). An air sample of 0.045 to 0.060 m<sup>3</sup> was adequate to obtain the desired quantity of boric acid. The absorber contents were transferred to a 50 ml. volumetric flask and water added to volume. A 2 ml. aliquot of this solution was pipetted into a small bottle and two drops concentrated hydrochloric acid added, followed by 10 ml. concentrated sulfuric acid. Then 10 ml. of 0.05% carmine in concentrated sulfuric acid were added and the solution set aside for 45 min. for color development. Two ml. of a blank solution and 2 ml. of a standard solution containing 10 micrograms of boric acid per ml. were each treated in the same manner. At the end of the color development periods, the optical densities of the sample and standard were read against the blank set to zero density in a Coleman spectrophotometer (Model 14) at a wave length of 585 mμ.

## D. Results.

1. Acute exposures, rats exposed 1-4 hours to concentrations of 52-492 mg./m<sup>3</sup> of diborane.

## a. Mortality.

Table I records the mortality fraction and time of death after gassing for rats exposed to Cts of 10,400 to 37,200 mg.min./m<sup>3</sup>. The majority of the deaths occurred within five days after exposure. When the Ct value was high and particularly at high chamber concentrations, there was an increased tendency for all deaths to occur shortly after gassing. For example, at the two highest diborane concentrations, 317 and 492 mg./m<sup>3</sup>, all animals exposed died within 2 hours after removal from the chamber.

## b. Toxic signs.

The principal toxic signs were respiratory in character. At higher concentrations the animals exhibited marked respiratory distress with dyspnea and short periods of apnea. Those animals exposed to the two highest diborane concentrations which died within 2 hours after gassing, experienced pronounced difficulty in breathing and showed marked gasping for air preceding death.

## c. Pathological examination.

The principal pathological changes were found in the lungs. Marked congestion and edema with areas of focal hemorrhage were observed uniformly. Liver, spleen and kidneys were not remarkable.

## 2. Chronic exposures.

Tables II and III summarize the mortality results and biochemical and hematological changes among animals chronically exposed to diborane for periods of three weeks to six months.

a. Test 1, dogs and rats, diborane concentration 6 mg./m<sup>3</sup>

## (1) Mortality.

During the course of the test both dogs and 17 of the 18 rats died. One dog died during the 10th exposure and the other after 25 exposures. Deaths of rats were distributed between the 7th and 113th exposures.

## (2) Toxic signs and biochemical and hematological changes.

No signs of toxic exposure, other than a mild rhinitis in some animals, were noted in the rats.

On the other hand, dogs exhibited marked symptoms of intoxication beginning with the first exposure. One dog, No. 70, was restless with rapid respiration which became normal on removal from the chamber. Shortly thereafter the dog developed diarrhea. After 5 exposures this dog appeared sluggish; he became anorexic after the seventh exposure and vomited prior to the ninth exposure. Rectal temperature at this time was 103.9°F. and respiratory rate 116/min. Total white cells were 16,000/cu.mm.; differential white count revealed 73% band form and 4.5% juvenile neutrophils in contrast with 6.8% band and no juvenile cells prior to gassing. After five hours of the tenth exposure dog No. 70 became apneic and died with blood and froth around the nares.

The second dog, No. 67, displayed similar toxic signs but to a lesser degree. During the ninth exposure the animal developed wheezing and irregular breathing. Prior to the tenth exposure the rectal temperature was normal, 101.1°F., but rose to 103.6°F. after gassing. By the twelfth exposure the dog appeared very ill and refused all food except milk. The animal then experienced a partial recovery until the sixteenth exposure at which time the dog developed anorexia, and the respiratory rate rose to 140/min. After the twenty-fifth exposure the dog was extremely weak and emaciated and died during the weekend. After 15 exposures, band form neutrophils increased from 13.0% of the total white cell count to 68.5%. The percentage then decreased to 53% after 20 exposures and 34.5% after 25 exposures, prior to death.

**(3) Pathological Examination.**

**(a) Rats.**

Examination of animals sacrificed after four weeks or less of diborane exposure revealed no changes attributable to the agent. Chronic tracheitis and chronic bronchitis were found in both control and experimental animals. Other tissues of the animals in the two groups were similar.

**(b) Dogs.**

Dog No. 70, which died during the tenth exposure, was autopsied immediately after death; dog No. 67, which died during a weekend, was not examined pathologically.

Examination of the respiratory tract of dog No. 70 showed acute and chronic nasopharyngitis, acute tracheitis, chronic bronchitis and confluent bronchopneumonia. The heart was normal and there was congestion of the liver and kidneys. These changes are consistent with secondary pneumonia following diborane exposure.

0.8-1.7 mg./m<sup>3</sup> b. Test 2, dogs, rats and guinea pigs, diborane concentration

**(1) Mortality.**

**(a) Dogs.**

Dog No. 44 died after 14 exposures while dog No. 15 survived the complete series of 130 exposures.

**(b) Rats and guinea pigs.**

In a group of 10 rats exposed 21 times 5 were dead after 18 exposures. In a second group of ten rats exposed 60 times 5 animals died between the 22nd and 28th exposures. None of 10 guinea pigs died during 95 exposures.

**(2) Toxic signs and biochemical and hematological changes.**

Symptoms of exposure in these dogs were much less pronounced than those in Test 1. After 9 exposures both dogs developed hyperpnea and anorexia. Despite a change in diet to raw meat to stimulate appetite, dog No. 44 gradually lost weight and appeared sluggish and ill. On the morning following the 14th exposure this animal was found dead in his cage. The weight of dog No. 15 did not change appreciably throughout the experiment. However, on a number of occasions both in and out of the gassing chamber, this animal experienced periods of hyperpnea.

No biochemical or hematological changes were noted in these animals.

(3) Pathological Examination.

(a) Dogs.

Dog No. 15 was sacrificed at the conclusion of the experiment. Post mortem changes in dog No. 44 prevented the performance of a satisfactory autopsy.

Tissues of dog No. 15 were compared with those from a control animal. The lungs of the control dog showed moderate chronic bronchitis. The kidneys, liver and colon of the control were not remarkable; the bladder revealed chronic cystitis. Chronic bronchitis and occasional areas of patchy atelectasis were found in the lungs of dog No. 15. The heart, kidneys, liver, colon and bladder were not remarkable. Pathological findings in the experimental dog did not appear to be due to diborane exposure.

(b) Rats.

Comparison with control rats of animals sacrificed after 57 exposures revealed no changes in the lungs, kidneys or liver of the experimental animals which were not found to a comparable degree in the controls.

(c) Guinea pigs.

Guinea pigs were sacrificed after 95 exposures and their tissues compared with those of the control animals. The lungs, kidneys, liver and spleen of the experimental animals were not remarkable in comparison with the controls except for the occurrence of occasional small focal hemorrhages in the lungs of some of the guinea pigs exposed to diborane. These are regarded as of doubtful significance and are probably not due to diborane.

IV. DISCUSSION.

Since diborane reacts readily with water (17) the possibility that a portion of the diborane may have been hydrolyzed in the chamber before inhalation must be considered. In a study of this problem, Feinsilver (19) showed that under conditions of this experiment vapor phase hydrolysis of diborane was negligible.

Death in rats following acute exposure to diborane is apparently due to severe pulmonary edema with congestion and focal hemorrhages of the lungs. Chronic exposure of two dogs to concentrations of 6 mg./m<sup>3</sup> resulted in death in both animals after the 10th and 25th exposures, respectively. The clinical picture preceding death was similar in both instances. At about the ninth exposure both animals developed anorexia, fever, increased respiratory rate and leukocytosis, with increase of band form neutrophils to 70% of the total white cells. Pathological examination of the first dog, which died at this time, revealed changes consistent with the occurrence of pneumonia secondary to lung injury. The second dog experienced a partial recovery and died about two weeks later. Pathological examination of this animal was not possible.

Seventeen of 18 rats exposed to a concentration of 6 mg./m<sup>3</sup> died during the course of six months diborane exposure. No pathological changes attributable to the agent were found in rats sacrificed after four weeks of

exposure to this concentration. Pathological examination of animals dying following exposure for longer periods of time was not performed. However, the nearly 100% mortality in this group of animals is strong indication of the chronic toxicity to rats of a concentration of 6 mg./m<sup>3</sup> of diborane.

No pathological changes were found in rats, guinea pigs, or one dog exposed chronically to diborane at concentrations of 0.8-1.7 mg./m<sup>3</sup> for one to six months. However, in view of the apparent tendency of concentrations of 6 mg./m<sup>3</sup> of diborane to cause secondary pneumonia in dogs and the high mortality among rats exposed for six months to this concentration, it is suggested that a diborane concentration of less than 0.8 mg./m<sup>3</sup> or 1 ppm be established as the maximum allowable concentration for chronic exposure of man.

Although the present experiments are not concerned primarily with the study of the mechanism of toxicity of diborane, they do provide evidence by which the validity of hypothesis of toxic action may be judged. In particular, the ease with which diborane is hydrolyzed to boric acid suggests the possibility that the toxicity of diborane may be due largely to the formation of boric acid in the body. However, the wide disparity between the amount of boric acid required to cause death in various animal species (20) and that which would be formed in the animal through hydrolysis of inhaled diborane does not support this hypothesis. Death from inhalation of diborane in animals occurs following exposure to concentrations of this gas which are sufficient to yield only a fraction of the amount of boric acid which has been reported as constituting a lethal dose. Consequently the toxicity of diborane must be attributed to a direct action of the material on the animal organism rather than to the secondary formation of boric acid.

## V. CONCLUSIONS.

### 1. Acute exposures.

Mortality fractions of 33 to 100% were observed. As the concentration of diborane is raised there is an increasing tendency for deaths of animals to occur at short periods of time after gassing. At the two highest concentrations, 317 and 492 mg./m<sup>3</sup>, all animals died within two hours after removal from the gassing chamber.

### 2. Chronic exposures.

a. Exposure to 6 mg./m<sup>3</sup> of diborane resulted in death of two dogs after 10 and 25 exposures, respectively. Both dogs developed clinical signs of respiratory infection at about the ninth exposure; this diagnosis was confirmed by autopsy of the first dog.

Seventeen of 18 rats died during the course of six months exposure; deaths were distributed between the 7th and 113th exposures.

b. One dog died after 14 exposures to 0.8-1.7 mg./m<sup>3</sup> of diborane; the other survived six months of exposure. Pathological examination of the second dog revealed no changes attributable to diborane exposure.

None of 10 guinea pigs died during 95 exposures. Examination of animals sacrificed after 95 exposures did not reveal any changes attributable to diborane exposure.

Pathological examination of rats sacrificed after 57 exposures revealed no changes not present to a comparable degree in the control animals.

c. It is suggested that the maximum allowable concentration for chronic exposure of man to diborane be less than  $0.8 \text{ mg./m}^3$  (1 ppm).

TABLE I

Acute Toxicity of Diborane by Inhalation to Rats  
(Six animals exposed at each concentration.)

Chamber Concentration		Exposure Time	Ct	No. of Deaths	Time of Death Days After Gassing			
$\text{mg./m}^3$	ppm	min.	$\text{mg.min./m}^3$		1	2-5	6-9	10-14
52	47	240	12,500	2	0	0	2	0
66	60	240	15,800	5	5	0	0	0
74	67	240	17,800	6	0	3	0	3
78	71	240	18,700	3	1	2	0	0
79	72	240	19,000	5	0	5	0	0
80	72	240	19,000	6	0	4	0	2
91	82	240	21,800	6	4	1	1	
107	97	240	25,700	3	3	0	0	0
123	111	240	29,500	6	6			
155	140	240	37,200	6	5	1	0	0
174	158	60	10,400	5	1	4	0	0
176	159	120	21,100	3	0	3	0	0
248	225	60	14,900	5	5	0	0	0
252	228	120	30,200	6	5	1		
317	287	60	19,000	6	6*			
492	446	60	29,500	6	6*			

\*All deaths occurred within two hours after removal from gassing chamber.

TABLE II

Chronic Exposure of Dogs, Rats and Guinea Pigs for Three Weeks to Six Months to Low Concentrations of Diborane

Test No.	Total Hours Exposed	Average Concn. of Diborane	Animals Exposed		Mortality Fraction	Distribution of Deaths Number of Exposures			
		$\text{mg./m}^3$	Species	No.		1-30	31-60	61-90	91-130
1	720	6	rats	18	17/18	6	4	4	3
	150	(5 ppm)	dogs	2	2/2	2			
2	126	0.8-1.7 (1-2 ppm)	rats	10	5/10	5			
	360		rats	10	5/10	5	0		
	780		dogs	2	1/2	1	0	0	0
	570		guinea pigs	10	0/10	0	0	0	0

TABLE III-A

Blood and Urine Analyses of Dogs During Chronic Exposures to Diborane Vapor - Test 1 (5 ppm)

	Control Dog						Dog #67						Dog #70					
	Weeks						Weeks of Exposure						Weeks of Exposure					
	Initial Value	1	2	3	4	5	6	Before Exposure	1	2	3	4	5	6	Before Exposure	1	2	3
I. Blood Counts																		
1. Red cells (millions)	5.7	6.1	6.6	5.0	6.6	9.4	6.0	5.0	5.9	6.0	5.0	7.6	7.3	7.7	5.0	5.9	5.9	5.7
2. White cells (thousands)	7.4	10.0	8.0	9.0	10.0	10.0	7.0	11.4	12.0	0.0	17.0	12.0	6.0	12.0	9.5	19.0	11.0	16.0
3. Differential																		
a. Eosinophil (%)	13.7	11.0	6.5	17.5	6.5	14.0	2.0	13.0	7.0		1.0	6.5	4.0		9.5	5.5	3.5	
b. Juvenile (%)	0.6										1.5	3.5	2.5				4.5	
c. Bands (%)	7.4	7.5	5.0	11.5	5.0	3.0	1.0	13.0	5.0		60.5	53.0	34.5		6.0	12.0	73.0	
d. Polymorphonuclear (%)	57.8	61.0	72.5	53.5	50.0	66.0	66.0	43.6	50.5		15.5	19.5	43.0		49.5	59.5	7.0	
e. Lymphocytes (%)	10.0	3.5	9.0	12.0	9.0	16.0	31.0	21.0	20.5		6.5	16.5	16.0		13.3	20.5	11.0	
f. Monocytes (%)	7.6	12.0	5.5	5.5	5.5	12.0	1.0	11.9	17.0		7.0	1.0	0.0		15.0	2.5	1.0	
II. Whole Blood Analyses																		
1. Hemoglobin (g. %)	14.5	16.1	17.6	16.3	16.7	13.0	17.6	15.9	16.1	16.4	14.7	10.6	16.1	15.4	15.5	16.6	16.2	15.8
2. Sedimentation rate (mm./hr.)	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	2.0	1.5	0.0	16.7	0.0	0.0	0.0	3.0	0.0
3. Hematocrit (%)	53.0	49.0	55.5	53.3	56.0	51.6	54.9	52.0	47.7	43.4	50.0	49.8	43.0	53.0	56.1	51.0	52.0	53.2
4. Specific gravity	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.05	1.06	1.06	1.06	1.06	1.06	1.06
5. Total Protein	7.6	5.5	6.6	6.2	6.3	5.7	5.3	7.6	5.9	6.8	7.0	6.7	5.9	7.3	7.4	5.7	7.2	6.7
III. Plasma																		
1. Specific gravity	1.03	1.02	1.02	1.02	1.02	1.02	1.02	1.03	1.02	1.03	1.03	1.02	1.02	1.03	1.03	1.02	1.03	1.03
IV. Serum Analyses																		
1. Chloride (mEq./l.)	100.3	93.3	124.7	105.0	119.0	122.0	113.6	102.9	119.7	117.1	106.5	116.4	122.0	120.6	103.4	114.5	123.4	115.5
2. Sugar (mg. %)	106.4			101.1	64.6	90.3	151.0	106.6	80.4		114.5	93.1	123.3	33.1	103.1	63.7		90.9
3. Urea (mg. %)	14.9				15.6	13.3	17.3	19.3				12.9	11.3	10.2	16.3			
4. Cholesterol (mg. %)	140.5	12.0	102.3		207.0	9.0		140.1	10.9	96.8	96.5	195.0	90.4		132.0	33.4	136.7	213.0
5. Calcium (mg. %)		2.9			9.2	3.3			3.5			10.3	11.2		19.6	4.2		
6. Phosphorus (mg. %)					3.7							5.3	7.3					
V. Urine Analyses*																		
1. pH	7.4	6.3	0.0			7.0	0.0	7.9	7.4	5.9			0.1	7.0	7.3		5.6	
2. Specific gravity	1.05	1.03	1.06			1.04	1.06	1.06	1.04	1.05			1.04	1.06	1.05		1.04	
3. Albumin	++	-	+++			-	+	+	-	++			-	-	++	+	+	+
4. Sugar	++	-	+++			-	+	+	-	++			-	-	++	+	+	+
5. Microscopic																		
a. Red blood cells	+							+							+	+	+	
b. White blood cells	+							+							+	+	+	
c. Bladder epithelial cells	+							+							+	+	+	
d. Renal epithelial cells	+							+							+	+	+	
e. Casts	+							+							+	+	+	

\* + positive, - negative, ± doubtful positive



TABLE III-B

Blood and Urine Analyses of Dogs During Chronic Exposures to Diborane Vapor - Test 2 (1-2 ppm)

	Control Dog										Dog #15										Dog #44	
	Weeks										Weeks of Exposure										Weeks of Exposure	
	4	8	12	16	20	24	28	Before Exposure		4	8	12	16	20	24	28	Before Exposure		4	8	Before Exposure	
I. Blood Counts																						
1. Red cells (millions)	6.9	6.6	9.9	9.3	2.8	3.6	2.8	7.5	7.4	7.8	7.8	8.3	7.2	7.2	7.2	8.0	7.5	7.4	7.8	7.2	7.3	6.9
2. White cells (thousands)	10.1	11.6	10.5	13.4	11.2	10.4	10.4	16.5	11.5	16.7	13.8	17.9	13.4	10.4	10.4	10.6	16.5	11.5	16.7	10.4	10.0	10.0
3. Platelet (thousands)	161.5	180.1	191.1		163.4	152.5	152.3	97.2	335.1	300.9		264.9	204.2	155.2	158.6		97.2	335.1	300.9	204.2	690.3	
4. Differential																						
a. Eosinophil (%)	11.8	7.2	9.9	9.3	2.8	3.6	2.8	4.6	3.7	2.8	4.5	6.8	2.4	0.0	0.0	3.5	4.6	3.7	2.8	2.4	6.6	3.3
b. Basophil (%)	0.0	0.1	0.4	0.3	0.5	0.5	1.2	0.0	0.0	0.3	0.3	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.3	0.1	0.0	0.0
c. Myelocyte (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
d. Juvenile (%)	0.7	1.6	0.9	0.2	1.5	1.4	2.1	0.7	1.2	1.2	0.5	0.3	1.3	0.9	0.2	0.2	0.1	0.7	1.2	0.9	0.1	1.7
e. Bands (%)	11.2	3.9	2.8	7.5	3.6	2.1	1.2	8.0	6.0	3.5	1.6	3.5	1.3	3.6	2.0	2.0	8.0	6.0	3.5	1.3	2.8	6.5
f. Polymorphonuclear (%)	50.2	56.6	61.5	51.8	63.5	54.3	60.0	62.6	69.0	70.3	71.1	67.8	65.0	63.0	70.0	70.0	62.6	69.0	70.3	65.0	52.6	57.5
g. Lymphocytes (%)	17.2	23.3	19.9	26.3	22.4	35.7	31.5	21.5	17.0	18.0	16.5	18.6	26.1	27.8	20.2	20.2	21.5	17.0	18.0	26.1	36.1	24.0
h. Monocytes (%)	1.0	9.1	3.4	4.5	5.5	1.9	1.5	3.0	2.2	4.0	5.5	2.6	4.3	4.0	4.0	4.0	3.0	2.2	4.0	4.3	1.0	6.3
II. Whole Blood Analyses																						
1. Hemoglobin (g. %)	13.9	14.0	15.0	15.2	14.7	15.2	15.1	14.7	16.6	14.2	15.6	15.3	14.1	14.0	17.2		14.7	16.6	14.2	15.3	15.7	16.6
2. Sedimentation rate (mm./hr.)	4.0	11.8	0.6	0.3	0.3	0.8	1.0	0.0	0.5	2.5	0.6	0.5	1.4	0.6	0.0		0.0	0.5	2.5	0.6	0.0	6.0
3. Hematocrit (%)	43.1	42.1	47.3	47.7	47.0	46.1	47.0	50.1	45.2	49.5	49.0	49.7	48.2	47.6	52.0		50.1	45.2	49.5	49.0	51.9	49.0
III. Serum Analyses																						
1. Chloride (mEq./l.)	118.1	115.8	115.1	115.1	115.5	116.5	110.3	116.6	114.1	130.0	124.3	110.6	116.3	113.3	117.5		116.6	114.1	130.0	124.3	120.7	111.5
2. Bicarbonate (mEq./l.)	24.5	24.0	26.2	24.7	26.0	28.4		26.2	26.2	29.0	27.3	27.8	27.0	28.3			26.2	26.2	29.0	27.3	27.8	22.3
3. Sugar (mg. %)	12.4	14.4	13.0	10.5	10.5	120.2	108.9	86.9	102.7	97.4	92.2	93.9	116.2	102.9			86.9	102.7	97.4	92.2	102.3	107.8
4. Urea (mg. %)	21.8	21.0	20.7	20.9	23.4	22.0	21.0	16.6	12.4	17.1	16.3	20.5	3.3	9.5			16.6	12.4	17.1	16.3	16.9	17.3
5. Potassium (mg. %)																						
6. Sodium (mg. %)																						
7. Calcium (mg. %)	11.9	12.0	12.6	11.7	9.9	380.9	378.6	376.9	12.0	11.4	11.0	303.3	383.8	381.0	405.0		376.9	12.0	11.4	11.0	381.2	11.0
8. Phosphorus (mg. %)	4.4	5.4	4.1	3.9	3.6	3.9	3.9	10.5	4.9	5.9	5.6	4.0	3.3	3.2	3.5		10.5	4.9	5.9	5.6	10.1	4.0
9. Cholesterol (mg. %)								100.0	147.9	114.9	155.9	184.1	219.7				100.0	147.9	114.9	155.9	184.1	159.0
IV. Urine Analyses*																						
1. pH	6.60	6.70	7.90	7.0	7.27	6.80	7.20	6.65	8.15	6.25	6.50	7.00	7.65	6.70			6.65	8.15	6.25	6.50	7.65	7.2
2. Specific gravity	1.03	1.02	1.03	1.03	1.03	1.03	1.03	1.04	1.03	1.04	1.04	1.03	1.03	1.04			1.04	1.03	1.04	1.03	1.04	1.04
3. Albumin	-	±	±	+	+	+	+	-	-	-	-	-	-	-			-	-	-	-	++	+++
4. Sugar	+	±	+	-	-	±	±	-	±	+	+	+	+	+			-	±	+	+	±	±
5. Microscopic																						
a. Red blood cells		+	+	+	+	+	+	+	+	++	+	+	+	+			+	+	++	+	+	+
b. White blood cells		++	+	+	+	+	+	+	+	+	+	+	+	+			+	+	+	+	+	+
c. Bladder epithelial cells	+		+	+	+	+	+	+	+	+	+	+	+	+			+	+	+	+	+	±
d. Renal epithelial cells	±		+	+	+	+	+	+	+	+	+	+	+	+			+	+	+	+	+	++
e. Casts		±				+					+	+	+	+					+	+	+	+

\* + positive, - negative, ± doubtful positive

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VII. BIBLIOGRAPHY.

1. Terlizzi, P.M., E. L. Klein. 1947. Diborane, Power Plant Memorandum No. 21, Part I. Technical Command Library, File No. ETF 285-87/PM21.
2. Dow, R. B. 1948. Editor, Ad Hoc Committee of the Inter-Bureau Technical Committee 2 February. Technical Command Library File No. ETF 285-109.
3. McAleir, B. A. Letter dated 14 March 1950, Mine Safety Appliance Co., Pittsburgh, Pa.
4. Spicer, S.S., R. F. Sievers and E. M. Russ. Project No. 222, Reports 1 and 2, USPHS, Washington, D.C.
5. Rozendaal, H. M. 1951. Clinical observations on the toxicology of boron hydrides. Archives of Industrial Hygiene and Occupational Medicine, 4: 257-260.
6. ACC Conf. Ltr. Nc 56/5721, Serial 019-49, 15 July 1949 to Bu Med with Bu Med, 1st Ind of 15 July 1950.
7. Van Slyke, D.D., R. A. Phillips, V. P. Dole, P. B. Hamilton, R. M. Archibald, and J. Plazin. 1950. Calculation of hemoglobin from blood specific gravities. J. Biol. Chem., 133: 349.
8. Sendroy, J., Jr. 1937. Microdetermination of chloride in biological fluids, with solid silver iodate. II. Titrimetric analysis. J. Biol. Chem., 120: 405.
9. Van Slyke, D.D. 1922. Studies of acidosis. XVIII. Determination of the bicarbonate concentration of the blood and plasma. J. Biol. Chem., 52: 495.
10. Folin, O. and H. Malmros. 1929. An improved form of Folin's micro method for blood sugar determinations. J. Biol. Chem., 83: 115.
11. Natelson, S., M. L. Scott and C. Beffa. 1951. A rapid method for the estimation of urea in biologic fluids, by means of the reaction between biacetyl and urea. Am. J. Clin. Path., 21: 275.
12. Natelson, S. 1950. Routine use of the Perkin-Elmer Flame Photometer in the clinical laboratory. Am. J. Clin. Path., 20: 463.
13. Zuckerman, J. L. and S. Natelson. 1948. A convenient and rapid procedure for total cholesterol estimation using an acid chloroform extraction. J. Lab. & Clin. Med., 33: 1322.

14. Kamlet, J. 1937. A combined microdetermination of calcium and phosphorus in blood serum. J. Lab. & Clin. Med., 22: 966.
15. Van Slyke, D. D., A. Hiller, R. A. Phillips, P. B. Hamilton, V. P. Dole, R. M. Archibald and H. A. Eder. 1950. The estimation of plasma protein concentration from plasma specific gravity. J. Biol. Chem., 183: 331.
16. Turner, A. 1946. A micro method for determination of hemoglobin. Bull. U. S. Army Med. Dept., 5: 605.
17. Schlesinger, H. I. and A. B. Burg. 1942. Recent developments in the chemistry of the boron hydrides. Chem. Revs., 31: 1.
18. Hatcher, J. T. and L. V. Wilcox. 1950. Colorimetric determination of boron using carmine. Anal. Chem., 22: 567.
19. Feinsilver, L. 1953. Quantitative determination of diborane in air. MLRR No. 170.
20. Pfeiffer, C. C. 1950. The pharmacology of boric acid and boron compounds. Bull. Natl. Formulary Comm., 18: 57.

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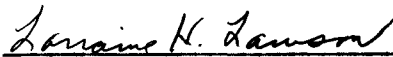
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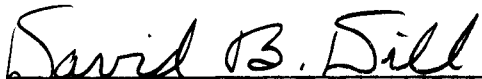
  
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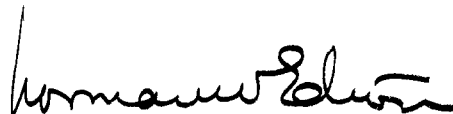
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7. Diborane, physiol. effects, symptoms
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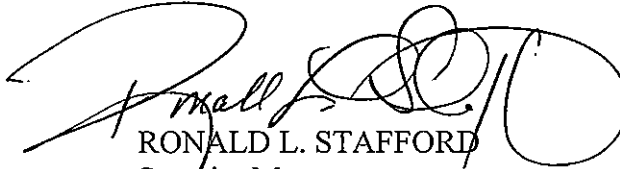
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b. Comstock, C.C.; Feinsilver, L.; Lawson, L.H.; Oberst, F.W. *Inhalation Toxicity of Diborane in Dogs, Rats, and Guinea Pigs*; Medical Laboratories Research Report No. 258; Chemical Corps Medical Laboratories: Army Chemical Center, MD, 1954, Unclassified, Distribution C. **ADB032228 CBRNIAC-CB-113261**

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